Amendments to the Specification

The specification has been amended to reflect the amendments that were entered in the parent application and to provided a related application paragraph. In addition, minor typographical errors were corrected. No new matter has been added.

Claim Amendments

Claims 1-9 and 11-22 have been cancelled. Claim 10 has been amended. New claims 23-34 have been added.

Claim 10 has been amended to recite that an array of diverse small ligand molecules are prepared. Support for the amendment can be found at page 2, lines 17-20.

Claims 23-26 and 28 recite the modified supports of Claims 5-9 as originally filed in the parent application. Support for the method steps recited in Claim 23 can be found at page 2, lines 17-21 of the specification and throughout U.S. Patent No. 5,143,854, which is incorporated by reference at page 1, lines 31-32 of the present specification.

Support for Claims 27 and 29 can be found, for example, at page 14, lines 12-15.

Support for Claims 30 and 31 can be found, for example, at page 6, lines 15-21.

Support for Claim 32 can be found, for example, in Claim 10 as originally filed and at page 2, lines 17-21, page 6, lines 3-25, page 7, lines 21-32 and page 8, lines 6-18. Additional support can be found, for example, at column 8, line 60 to column 9, line 51 of U.S. Patent No. 5,143,854.

Support for Claim 33 can be found, for example, at page 8, lines 6-18.

Support for Claim 34 can be found, for example, at page 12, lines 21-24.

Instant Claims Are Novel and Unobvious

Applicants note that in U.S. Application No. 09/102,986 (the parent application), claims directed to the modified substrates recited in Claims 23-34 (Claims 5-9 of the parent application) have been rejected under 35 U.S.C. §§ 102 and 103 as being anticipated by or obvious over a number of cited references.

Applicants do not concede the propriety of these rejections. Notwithstanding this, none of the references cited in the parent application teach the use of these modified supports in

preparing an array of diverse polymers. The references cited by the Examiner as teaching such modified supports disclose preparing a single polymer on a modified support. Thus, the instant claims are not anticipated by the references cited in the parent application.

Moreover, it would not have been obvious to use one of the recited modified substrates to prepare an array of diverse polymers in view of the combined teachings of the cited references. One feature of the present modified substrates is that the linking groups can be cleaved under mild conditions, such as by treating a linking group with a thiol-cleaving reagent (e.g., dithiothreitol). None of the cited references teach that it is desirable to cleave ***an array of diverse polymers*** from a substrate. Thus, a method of preparing an array of diverse polymers using the recited modified substrate is not obvious over the references cited in the parent application.

CONCLUSION

In view of the above amendments and remarks, it is believed that all claims are in condition for allowance, and it is respectfully requested that the application be passed to issue. If the Examiner feels that a telephone conference would expedite prosecution of this case, the Examiner is invited to call the undersigned at (978) 341-0036.

Respectfully submitted,

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By _____

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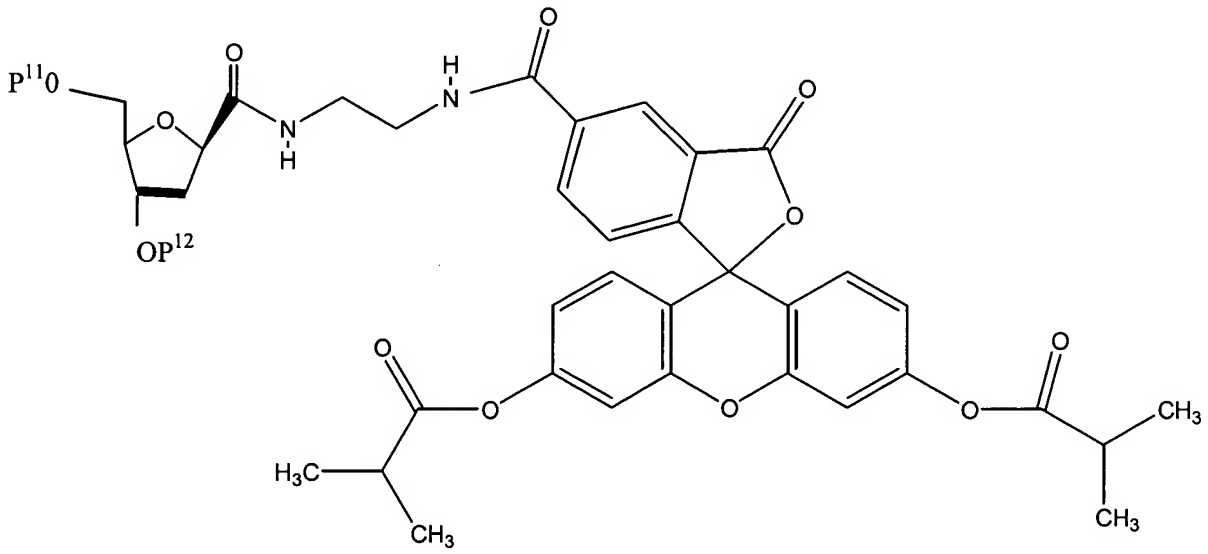
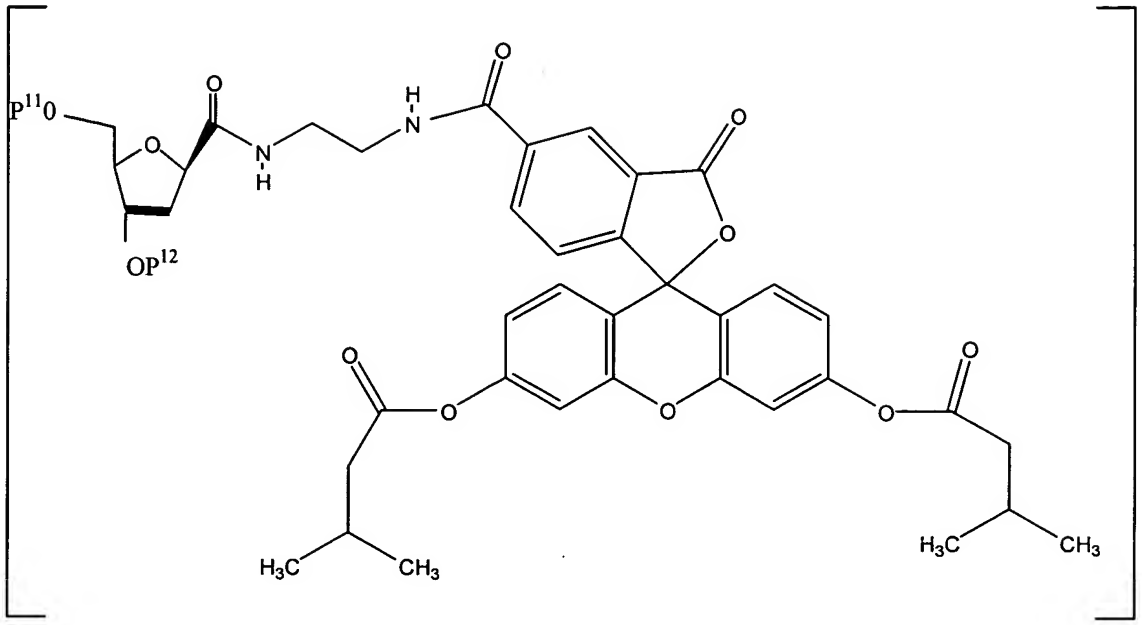
MARKED UP VERSION OF AMENDMENTS

Specification Amendments Under 37 C.F.R. § 1.121(b)(1)(iii)

Replace the paragraph at page 3, lines 12 through 17 with the below paragraph marked up by way of bracketing and underlining to show the changes relative to the previous version of the paragraph.

According to another aspect of the invention, a novel label is provided which can be incorporated into either the 3' or 5' terminus of a DNA oligomer. This label has the formula





wherein P^{11} and P^{12} are independently selected from the group consisting of hydrogen, a protecting group, and a phosphodiester-forming group.

Replace the paragraph at page 14, lines 7 through 18 with the below paragraph marked up by way of bracketing and underlining to show the changes relative to the previous version of the paragraph.

As shown in Fig. 1C, when N=2, the disulfide bond of **1** cleaves under neutral [netural] or basic conditions in the presence of DTT to give an oligonucleotide **2**, which possess the 2-mercaptoethyl [2-mercaptoehtyl] phosphate ester at the 3'-end. This ester fragments [have been observed] efficiently to produce the [3-phosphorylated] 3'-phosphorylated oligonucleotide **3**. This produce has been shown to be identical to that produced by the base catalyzed cleavage of oligonucleotides tethered to the surface via the known Phosphate-ON reagent (Glen Research). The unsymmetrical disulfide [disulfie] linker when N=2 is preferred when it is desirable to cleave from the surface and analyze the oligonucleotides by HPLC, since the resultant oligonucleotides do not possess a 3'-thiol appendage. In the cases where N>2, the mercaptoalkyl [mercpatoalkyl] esters should be more stable and the cleaved oligonucleotides retain the corresponding thiol

appendage. This makes subsequent analysis of the cleaved DNA [diffciult] more difficult because of oxidation [oxitation] of the thiol group.

Replace the paragraph at page 25, line 18 through page 26, line 2 with the below paragraph marked up by way of bracketing and underlining to show the changes relative to the previous version of the paragraph.

The oil was [combined with] dissolved in 50 mL of 20% THF in anhydrous MeOH and a catalytic amount of K_2CO_3 was added. The mixture was stirred at room temperature overnight. EtOAc (50 mL) was added and the resulting mixture was poured into 50 mL of saturated aqueous $NaHCO_3$. The layers were separated and the aqueous portion was extracted with two 50 mL portions of ethyl acetate. The combined organic portions were washed with saturated aqueous NaCl and dried over anhydrous Na_2SO_4. Evaporation of the solvent provided the crude product as an orange oil. Purification was carried out by flash chromatography (hexane/EtOAc, 3/7 with 1% triethylamine) to provide 2.65g (73% for the two steps) of product **16** as a pale yellow oil.

Claim Amendments Under 37 C.F.R. § 1.121(c)(1)(ii)

10. (Amended) A method of synthesizing an array of diverse small ligand molecules on a solid support having optional spacers, said small ligand molecules being removable therefrom upon treatment with a suitable disulfide cleaving reagent, said method comprising:

(a) contacting a solid support with an unsymmetrical disulfide linking group of formula:

$$P^1\text{-}X^1\text{-}(W^1)_n\text{-}S\text{-}S\text{-}(W^2)_m\text{-}X^2\text{-}P^2 \qquad \text{(IIb)}$$

wherein,

P^1 and P^2 are each members independently selected from the group consisting of a hydrogen atom, an activating group and a protecting group;

X^1 and X^2 are each independently selected from the group consisting of a bond, -O-, -NH-, -NR- and $-CO_2-$, wherein R is a lower alkyl group having one to four carbon atoms;

W^1 and W^2 are each independently selected from the group consisting of methylene, oxyethylene and oxypropylene; and

n and m are each independently integers of from 2 to 12 with the proviso that n and m are not the same when W^1 and W^2 are the same,[;]

to produce a derivatived solid support having attached unsymmetrical disulfide linking groups suitably protected with protecting groups;

(b) optionally removing said protecting groups, if present, from said derivatized solid support to provide a derivatized solid support having unsymmetrical disulfide linking groups with synthesis initiation sites; and

(c) coupling said small ligand molecules to said synthesis initiation sites on said derivatized solid support to produce a solid support having an array of diverse small ligand molecules which are removable therefrom upon application of said disulfide cleaving agent.